

RIGID CAPSULE, AND ITS MANUFACTURE

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Abstract of JP2000202003

PROBLEM TO BE SOLVED: To easily manufacture a capsule without requiring a strict temperature control by forming the rigid capsule of a gel of polysaccharide selected from pullulan, hemicellulose, cornstarch, carboxymethyl cellulose and its water-soluble salt.

SOLUTION: This rigid capsule is formed of a gel of polysaccharide selected from pullulan, hemicellulose, cornstarch, carboxymethyl cellulose and its water-soluble salt. Then, in the rigid capsule, a filler article containing polyethylene glycol #200-#600, is filled. In this case, a pin for capsule forming is dipped in a capsule preparation liquid containing the polysaccharide selected from pullulan, hemicellulose, cornstarch, carboxymethyl cellulose and its water-soluble salt, and a gelling agent of the polysaccharide, and then, the pin is pulled up, and the capsule preparation liquid adhered to the pin is gelatinized and dried, and thus, the rigid capsule is manufactured.

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CLAIMS

[Claim(s)]

[Claim 1] The hard capsule characterized by consisting of gel of one sort chosen as a pullulan, a hemicellulose, corn starch, and a list from a carboxymethyl cellulose and its water-soluble salt, or two sorts or more of polysaccharide.

[Claim 2] The hard capsule according to claim 1 filled up with packing containing polyethylene-glycol #200-#600.

[Claim 3] The manufacture approach of the hard capsule characterized by the pin for capsule formation being immersed in the capsule preparation liquid containing one sort or two sorts or more of polysaccharide chosen as a pullulan, a hemicellulose, corn starch, and a list from a carboxymethyl cellulose and its water-soluble salt, and the gelling agent of this polysaccharide, and pulling up this pin subsequently, gelling the capsule preparation liquid adhering to this pin, and drying.

[Claim 4] The manufacture approach according to claim 3 that capsule preparation liquid is that in which xanthan gum and/or locust bean gum are included as the gelling agent with a pullulan.

[Translation done.]

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DETAILED DESCRIPTION

[Detailed Description of the Invention]

[0001]

[Field of the Invention] This invention relates to the non-gelatin hard capsule used for drugs, quasi drugs, food, etc.

[0002]

[Description of the Prior Art] Conventionally, as a hard capsule used for drugs, quasi drugs, food, etc., although the gelatin hard capsule is mainly used, the non-gelatin hard capsule is demanded in recently.

[0003] As a non-gelatin hard capsule, the hard capsule which makes water-soluble cellulose, such as hydroxypropyl methylcellulose, a basis is known conventionally (JP,3-279325,A).

[0004] However, although this hard capsule makes a basis the cellulose ether permuted by the alkyl group and the hydroxyalkyl radical, and this kind of cellulosic dissolves in low-temperature water, at an elevated temperature, it does not dissolve and the viscosity of the dissolution/dispersion liquid of these cellulose tends to be influenced of temperature, and if the temperature of the solution of the cellulosic which water was made to distribute at an elevated temperature is lowered gradually, viscosity will rise rapidly near 50 degree C.

[0005] Therefore, when manufacturing a hard capsule using the above-mentioned cellulosic, the temperature control of strict capsule preparation liquid is required.

[0006] Moreover, if the hard capsule cast with the above-mentioned cellulosic is filled up with polyethylene-glycol #200-#600 (PEG#200-#600) into this, it is observed that a polyethylene glycol oozes out on a capsule front face. On the other hand, the capsule filled up with the liquefied drug to the hard capsule is also put in practical use by development of the encapsulation machine for liquefied objects, and this seal machine as everyone knows in recent years. By the way, in ordinary temperature, although a liquefied polyethylene glycol (PEG#200-#600) has the solvent action which was excellent to the refractory drug and it is suitably used as an excipient, if the hard capsule cast with the above-mentioned cellulosic is filled up with these PEG#200-#600, it is observed that PEG oozes out on a capsule coat front face. For this reason, it is hard to fill up the hard capsule of the above-mentioned cellulosic with the contents containing polyethylene-glycol #200-#600.

[0007] This invention aims at offering easily the non-gelatin hard capsule in which capsule manufacture is possible, and its manufacture approach, without there being no exudation and moreover requiring a strict temperature control, even if it was made in view of the above-mentioned situation and filled up with polyethylene-glycol #200-#600.

[0008]

[The means for solving a technical problem and the gestalt of implementation of invention] this invention person did the knowledge of it being effective to manufacture a hard capsule by making a pullulan, a hemicellulose, corn starch, a carboxymethyl cellulose, or its water-soluble salt into a basis, as a result of inquiring wholeheartedly, in order to attain the above-mentioned purpose. That is, forming a good coat is known, for example, a pullulan, a hemicellulose, corn starch, a carboxymethyl cellulose, or its water-soluble salt coats the tabular matter or the tabular globular form matter etc. with the water solution of a

pullulan, and a coat will be formed if it is made to dry. However, when it is going to manufacture a capsule by the so-called dipping method as these solutions are also, before desiccation, the liquid of the above-mentioned macromolecule hangs down a pin, and falls, the homogeneity of a coat is not acquired, and molding of a good capsule cannot be performed. However, the knowledge of the ability to perform capsule manufacture good was carried out by blending the matter which is easy to gel by the temperature change as a gelling agent to the water solution of the above-mentioned macromolecule, and making the liquid of the above-mentioned macromolecule gel on a pin. Moreover, the knowledge of exudation not arising, even if it fills up with polyethylene-glycol #200-#600 the hard capsule formed of the gel of the above-mentioned giant molecule is carried out.

[0009] Therefore, the hard capsule characterized by this invention consisting of gel of one sort chosen as a pullulan, a hemicellulose, corn starch, and a list from a carboxymethyl cellulose and its water-soluble salt or two sorts or more of polysaccharide is offered. In this case, it fills up with packing with which this hard capsule contains polyethylene-glycol #200-#600 effectively.

[0010] Moreover, this invention is immersed in the capsule preparation liquid containing one sort or two sorts or more of polysaccharide chosen as a pullulan, a hemicellulose, corn starch, and a list from a carboxymethyl cellulose and its water-soluble salt, and the gelling agent of this polysaccharide in the pin for capsule formation, subsequently this pin is pulled up, and the manufacture approach of the hard capsule characterized by gelling the capsule preparation liquid adhering to this pin, and drying is offered.

[0011] Since the above-mentioned polysaccharide dissolves in the water solution of broad temperature, unlike a previous cellulosic, the relation between temperature and viscosity does not produce [a as rapid viscosity change as a previous cellulose] in the usual temperature requirement. However, if the macromolecule which adhered to the pin by adding a gelling agent in the water solution of these macromolecules is cooled, in order to gel rapidly A capsule can cast easily, this invention person's moldability of a capsule used to improve by adding the matter which is easy to gel by the temperature change to a pullulan, a hemicellulose, corn starch, a carboxymethyl cellulose, or its water-soluble salt, as a result of examining the moldability of a capsule, and the restoration nature of polyethylene-glycol #200-#600 about various giant molecules, as mentioned above, and it used to find out that restoration of polyethylene-glycol #200-#600 is still more possible.

[0012] Hereafter, if it explains in detail, the non-gelatin hard capsule of this invention will be a thing using per this invention and also one sort chosen as a pullulan, a hemicellulose, corn starch, and a list from water-soluble salts, such as alkali-metal salts, such as a carboxymethyl cellulose and its sodium salt, or two sorts or more of polysaccharide as a basis, and will be obtained by gelling this polysaccharide with a gelling agent.

[0013] A pullulan is Aureobasidium which starch is used as a raw material and is one sort of black yeast. It is alpha-1 which makes a unit the maltotriose which cultivated Pullulans and was obtained, and natural polysaccharide combined six times, and it is known as additives, such as food, drugs, and cosmetics, for many

years, and a commercial item can be used as a pullulan. The "hemi sirloin" made from the soybeans currently manufactured in FUJI OIL Co., Ltd. as a hemicellulose on the other hand is suitable, and it will not be limited especially if it is usually used for binders, such as drugs or health food, etc. about corn starch and a carboxymethyl cellulose.

[0014] The pin for capsule formation is immersed in per manufacture approach and also the capsule preparation liquid which dissolved the above-mentioned polysaccharide and a gelling agent when explained in full detail of a hard capsule which makes the above-mentioned polysaccharide of this invention a basis, and this is pulled up, and the capsule preparation liquid which adhered to the pin on this pin is gelled, and it dries.

[0015] Here, as for especially the concentration of the polysaccharide in the above-mentioned capsule preparation liquid, considering as 10 - 20% is desirable 5 to 30% (it is below the same% of the weight).

[0016] Moreover, as a gelling agent, the matter which is easy to gel by the temperature change is desirable, xanthan gum, locust bean gum, gellant gum, a carrageenan, a tamarind seed polysaccharide, pectin, curdlan, gelatin, a furcellaran, an agar, etc. can be mentioned, two or more sorts can be mixed and, specifically, these matter can also be used further.

[0017] Especially, for the pullulan, xanthan gum/locust bean gum, gellant gum, and a carrageenan are suitable. The quick capsule of the dissolution can be obtained by using gellant gum especially. As for especially the concentration of the above-mentioned gelling agent, considering as 0.1 - 1.0% is desirable 0.01 to 10% among capsule preparation liquid.

[0018] In addition, when the water-soluble compound which gives potassium ion, ammonium ion, and calcium ion as a gelation adjuvant, for example, potassium chloride, an ammonium chloride, ammonium acetate, a calcium chloride, etc. can be used when using a kappa carrageenan as a gelling agent, and using an IOTA carrageenan, the water-soluble compound which gives calcium ion, such as a calcium chloride, can be used.

[0019] Moreover, when using gellant gum as a gelling agent, the water-soluble compound which gives sodium ion, potassium ion, calcium ion, and magnesium ion, for example, a sodium chloride, potassium chloride, a calcium chloride, magnesium sulfate, etc. can be used as a gelation adjuvant, and an organic acid and its water-soluble salt, for example, a citric acid, or a sodium citrate can be used further.

[0020] When using the above-mentioned gelation adjuvant, especially a gelation adjuvant has 0.06 - 0.2% of desirable use 0.05 to 0.6% among capsule preparation liquid.

[0021] In addition, in this invention, optimum dose addition of the additive usually used for hard capsules, such as coloring matter and a pigment, may be carried out.

[0022] In this invention, although the above-mentioned polysaccharide, a gelling agent, and other request components are dissolved in water and capsule preparation liquid is obtained, there is especially no limit in the dissolution sequence of the component to water, polysaccharide may be dissolved first or a

gelling agent may be dissolved. Although especially a melting temperature is not restricted, either, 40-100 degrees C of things more preferably considered as 50-95 degrees C are recommended.

[0023] Although the temperature immersed in the pin for capsule formation is also selected suitably, it is desirable to consider as 40-60 degrees C especially 30-80 degrees C.

[0024] In addition, as for especially the viscosity of the capsule preparation liquid at the time of this pin immersion, it is desirable that it is 1,000 - 8,000 mPa-s 100 to 10,000 mPa-s.

[0025] Although it is desirable to carry out by cooling radiationally as for the gelation after pulling up a pin, stoving of it may be carried out to 40-80 degrees C after gelation.

[0026] Although the hard capsule of this invention obtained as mentioned above makes the above-mentioned polysaccharide a basis, it is desirable that it is especially the following presentation.

polysaccharide: -- 70% or more -- more -- desirable -- 80% or more and gelling agent: 0.01-30% -- more -- desirable -- 0.1 - 10%, and gelation adjuvant: 0-30% -- more -- desirable -- 5% or less and moisture: 1-20% -- more -- desirable -- 5 -

15%, and the sum total 100% [0027] The capsule by this invention is applicable to chemicals, fertilizer, etc. for an animal or vegetation including drugs or food. Especially as drugs, it is applicable also as the object for drugs administered orally, the container for inhalations, or suppositories. Furthermore, it is applicable also as the so-called quasi drugs aiming at disinfection, washing, etc. of a false tooth, glasses, a contact lens, etc.

[0028] In this case, since the capsule of this invention does not have exudation even if it is filled up with polyethylene-glycol #200-#600, it is effective in being filled up with various packing containing polyethylene-glycol #200-#600.

[0029] As other components with which the capsule of this invention can be filled up, In addition to the powder generally known, granulation, and a tablet, as alcohol/polyhydric alcohol, stearyl alcohol, cetanol, a polyethylene glycol, or its ester object is mentioned, fatty acids, such as citric-acid triethyl, such as sesame oil, soybean oil, peanut oil, corn oil, hardened oil, a paraffin oil, and white beeswax, a triacetin, stearin acid, a palmitic acid, and a myristic acid, and the derivative of those, for example, triglyceride etc., can be mentioned as fats and oils, and it is suitable for restoration of a liquid and the quality of a half-solid.

[0030]

[Example] Hereafter, although an example explains this invention concretely, this invention is not restricted to the following example.

[0031] [Example 1] Ethyl alcohol 1g was added to xanthan gum 0.3g and locust-bean-gum 0.3g, and 170g of water was made to distribute after that. This was warmed at 70 degrees C and pullulan 30g was dissolved. This was kept warm at 60 degrees C, after throwing in the pin for capsule formation, it took out, and it was made to dry and the capsule was produced.

[0032] The clarity-and-color-of-solution trial using 50ml of purified water warmed at 37**2 degrees C about the obtained capsule according to the clarity-and-color-of-solution examining method of a Japanese pharmacopoeia convention was

performed (the number of sample offering capsules three pieces). Consequently, dissolution time amount was 9.19 **0.39 minutes.

[0033] [Example 2] Gellant gum 1g was dissolved in 168g of about 90-degree C water. 1g of sodium citrates and pullulan 30g were dissolved in this. This was kept warm at 55 degrees C, after throwing in the pin for capsule formation, it took out, and it was made to dry and the capsule was produced. The result of having performed the clarity-and-color-of-solution trial like the example 1 was 6.41 **0.63 minutes.

[0034] [Example 3] Carrageenan 0.2g and 0.4g of ammonium chlorides were dissolved in 170g of about 70-degree C water. Pullulan 30g was dissolved in this. This was kept warm at 52 degrees C, after throwing in the pin for capsule formation, it took out, and it was made to dry and the capsule was produced. The result of having performed the clarity-and-color-of-solution trial like the example 1 was 8.17 **0.41 minutes.

[0035] [Example 4] Corn-starch 20g was dissolved in 179g of 95-degree C water. This was cooled at 50 degrees C and carrageenan 0.4g and 0.4g of potassium chloride were dissolved. This was succeedingly kept warm at 50 degrees C, after throwing in the pin for capsule formation, it took out, and it was made to dry and the capsule was produced.

[0036] [Example 5] Hemi sirloin 20g was dissolved in 179g of 80-degree C water. This was cooled at 50 degrees C and carrageenan 0.4g and 0.4g of potassium chloride were dissolved. This was succeedingly kept warm at 50 degrees C, after throwing in the pin for capsule formation, it took out, and it was made to dry and the capsule was produced. The result of having performed the clarity-and-color-of-solution trial like the example 1 was 5.93 **0.39 minutes.

[0037] [Example 6] Carboxymethylcellulose sodium 5g was dissolved in 194g of 80-degree C water. This was cooled at 50 degrees C and carrageenan 0.4g and 0.4g of potassium chloride were dissolved. This was succeedingly kept warm at 50 degrees C, after throwing in the pin for capsule formation, it took out, and it was made to dry and the capsule was produced. The result of having performed the clarity-and-color-of-solution trial like the example 1 was 9.20 **0.78 minutes.

[0038] [Example of an experiment] After being filled up with PEG#400 and saving for three days at 60 degrees C about the capsule of examples 1-6, visual inspection of the capsule by viewing was conducted and the result as shown in Table 1 was obtained (the number of sample offering capsules three pieces).

[0039]

[Table 1]

カプセル	外観		
	試料1	試料2	試料3
実施例1	○	○	○
実施例2	○	○	○
実施例3	○	○	○
実施例4	○	○	○
実施例5	○	○	○
実施例6	○	○	○
対照カプセル*1	△	△	×
対照カプセル*2	×	×	×

*1: Gelatine-capsule-*2-:-HPMC-capsule-O-:-change-less ** : although an appearance hardly changes, PEG#400 ooze from x:coat front face to which reinforcement falls. [0040]

[Effect of the Invention] According to this invention, restoration of polyethylene-glycol #200-#600 is possible for the capsule which could manufacture the non-gelatine capsule that a strict temperature control etc. is unnecessary and easily, and was obtained.

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